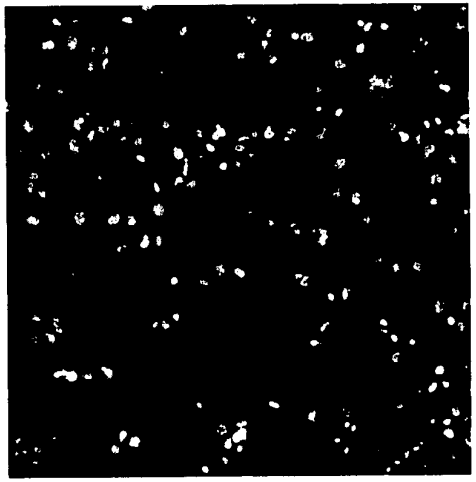
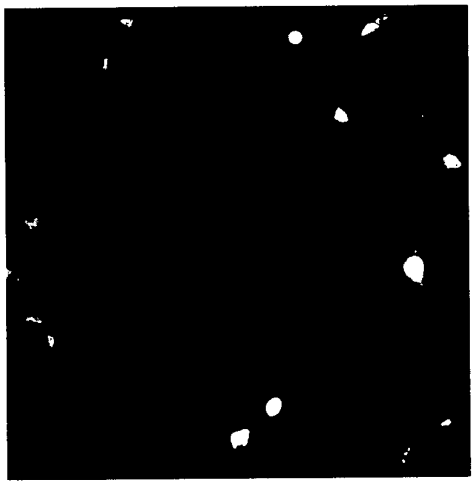
Figure 1



Hoechst 33342 Stain



Green Fluorescent Protein

Figure 2

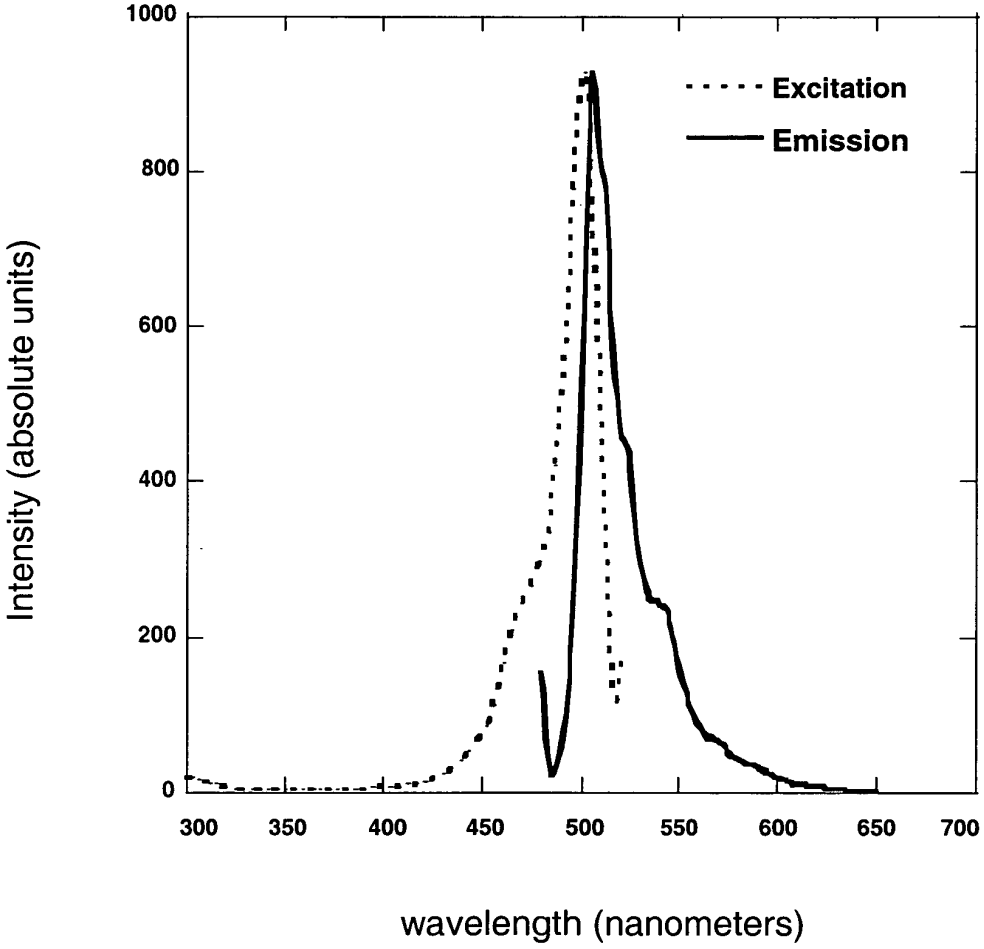

1000
800
600
400
200
0
300
350
400
450
500
550
600
650
700
Excitation
Emission
Intensity (absolute units)
wavelength (nanometers)

Figure 3

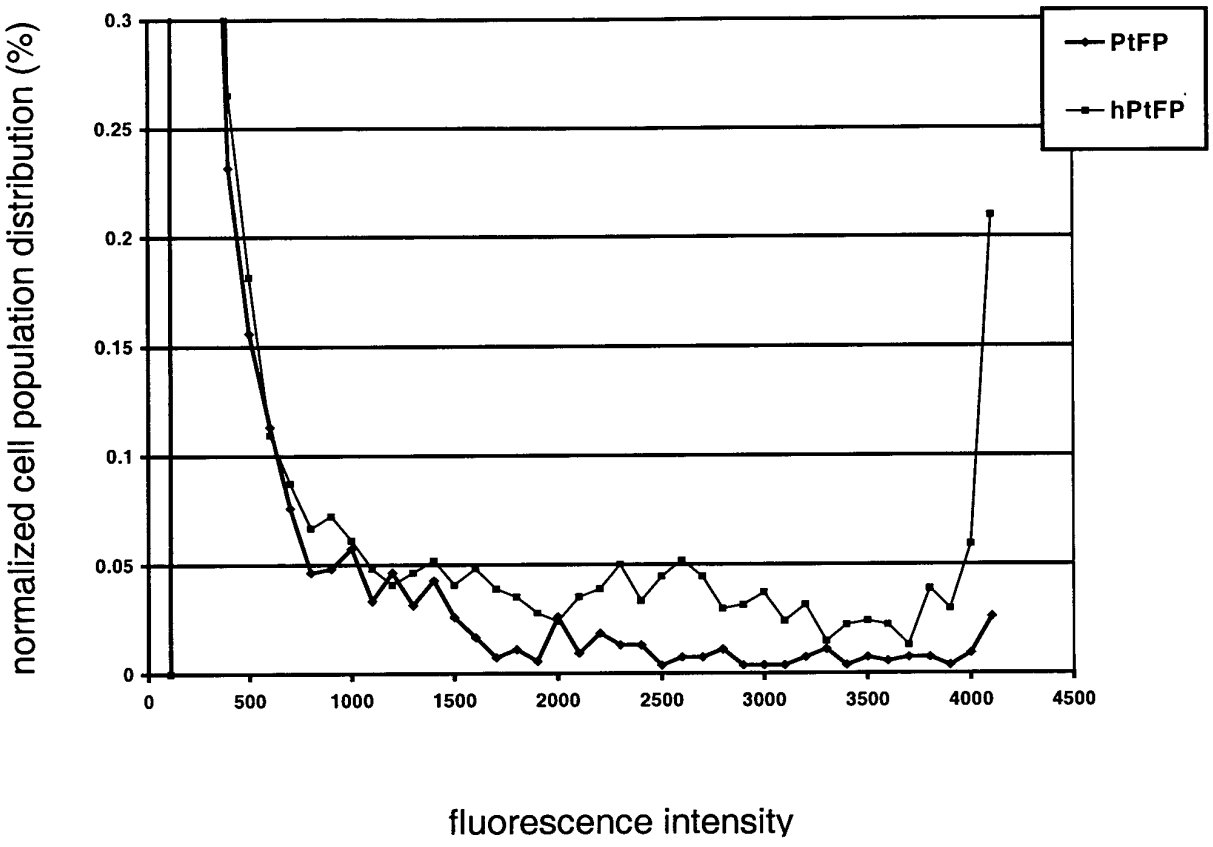
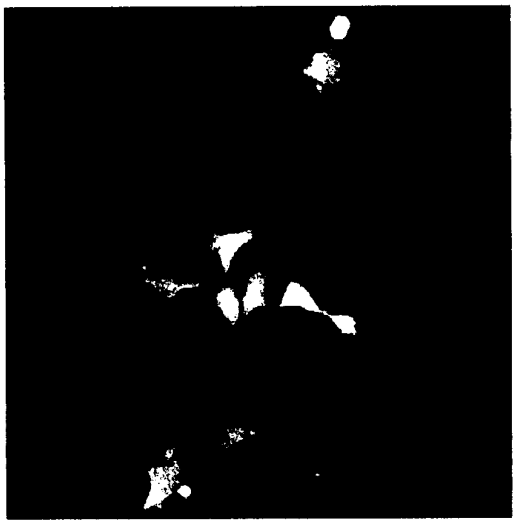
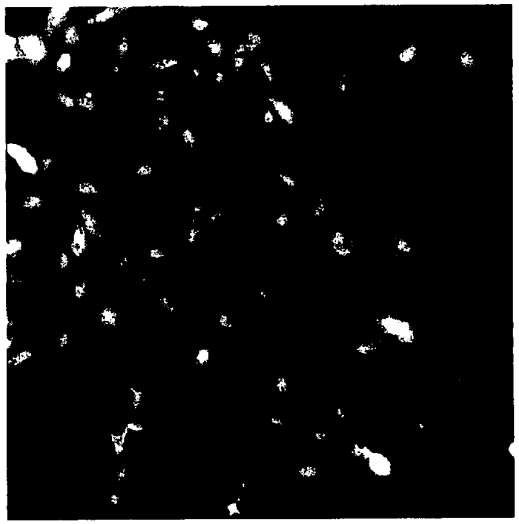

normalized cell population distribution (%)
0.3
0.25
0.2
0.15
0.1
0.05
0
0
500
1000
1500
2000
2500
3000
3500
4000
4500
PtFP
hPtFP
fluorescence intensity

Figure 4



HEK 293 cells



A549 cells

Figure 5

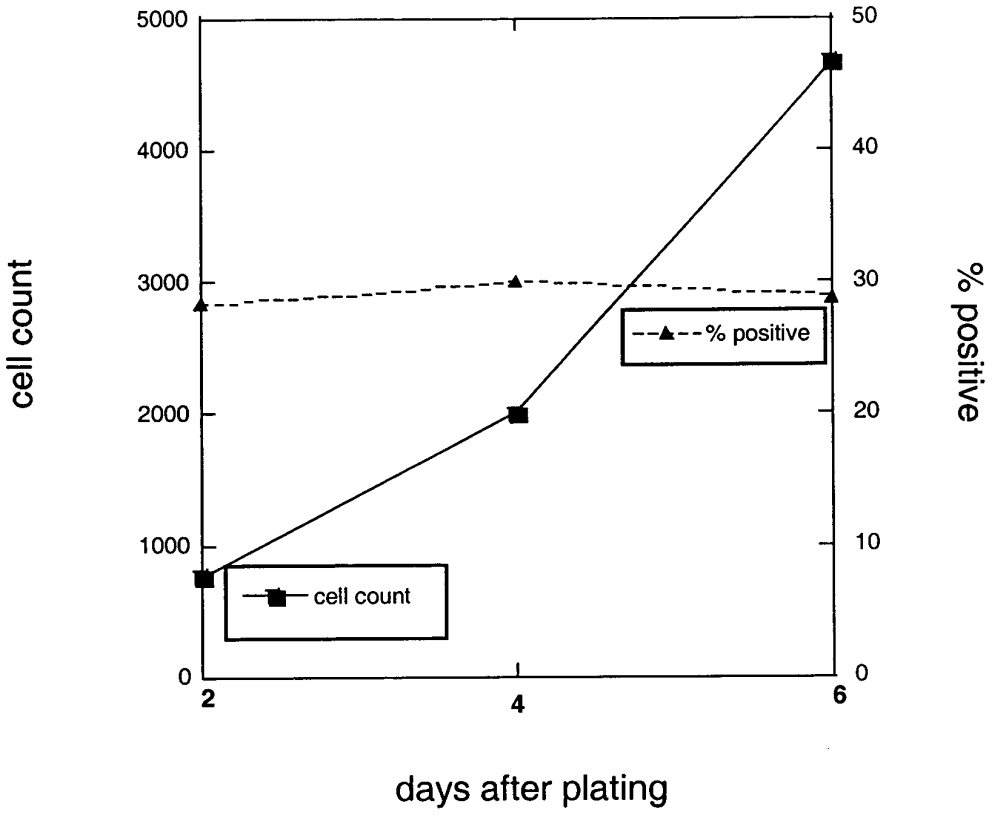
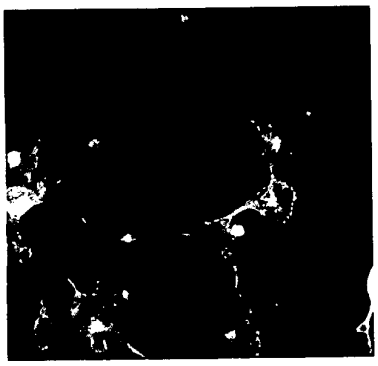
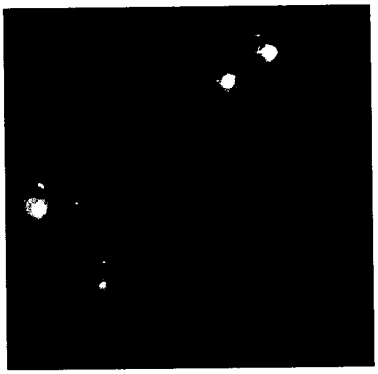

5000
4000
3000
2000
1000
0
cell count
50
40
30
20
10
0
% positive
% positive
cell count
2
4
6
days after plating

Figure 6

A



B



C

Figure 7

Caspase-3 biosensor

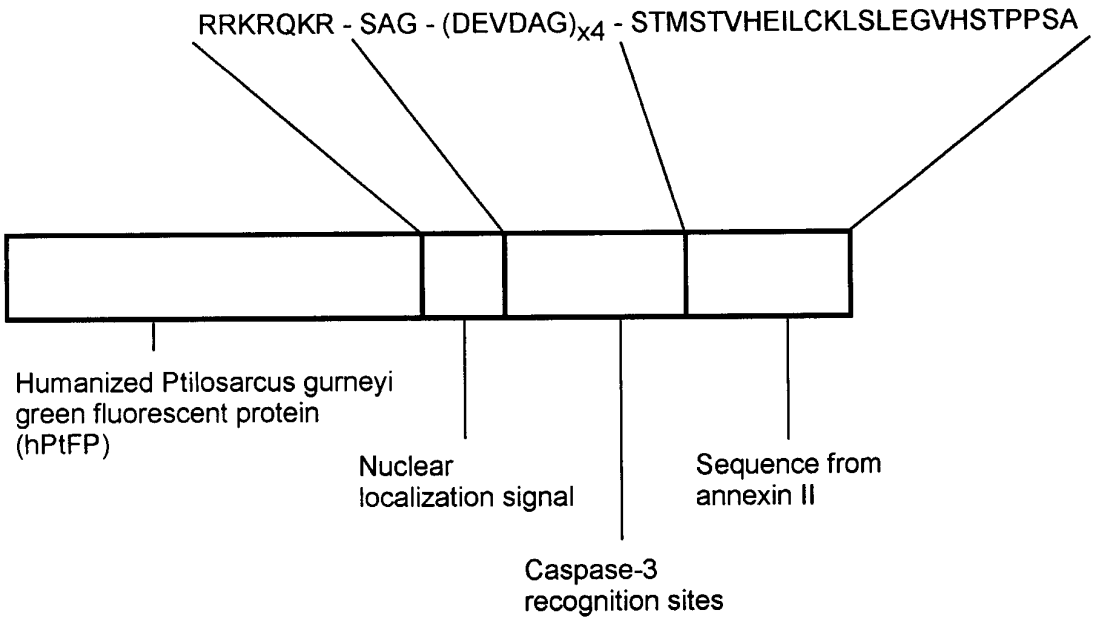


Figure 8

Caspase-8 biosensor

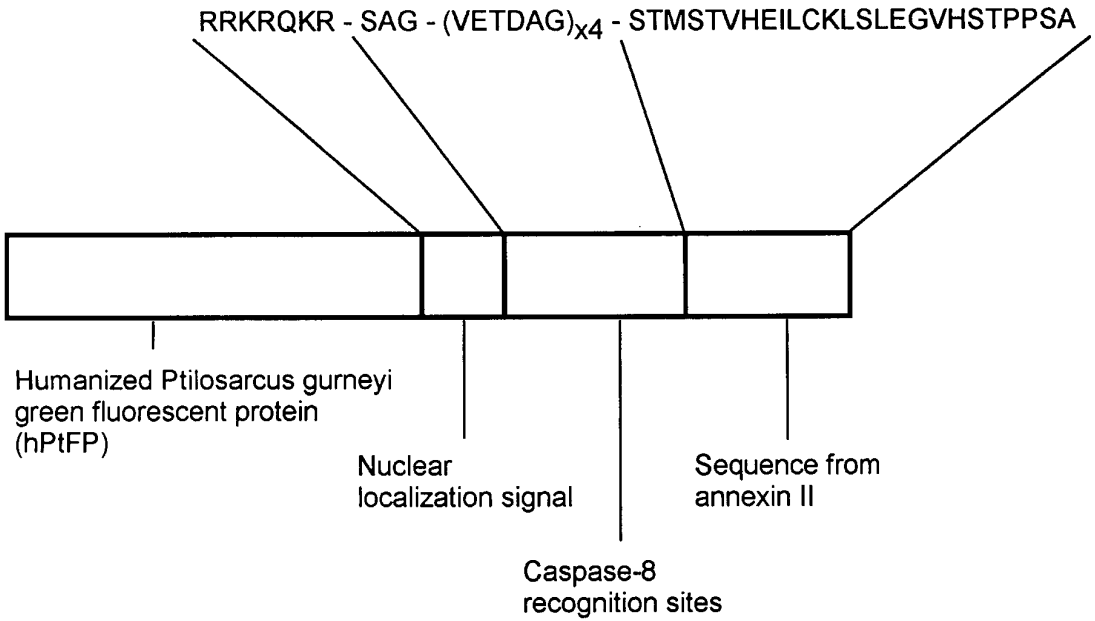


Figure 9

```
                Met
            Met Val
          +1          Asn Arg Asn Val Leu Lys Asn Thr Gly Leu Lys Glu Ile Met Ser Ala Lys Ala
PtFP       1      ATG AAC CGC AAC GTA TTA AAG AAC ACT GGA CTG AAA GAG ATT ATG TCG GCA AAA GCT
hPtFP      1  ATG GTG AAC CGG AAC GTG CTG AAG AAC ACC GGC CTG AAG GAG ATC ATG AGC GCC AAG GCC
               ***       *       * * *           *   *       *       *     ***   *   *   *

          +1 Ser Val Glu Gly Ile Val Asn Asn His Val Phe Ser Met Glu Gly Phe Gly Lys Gly Asn
PtFP      61  AGC GTT GAA GGA ATC GTG AAC AAT CAC GTT TTT TCC ATG GAA GGA TTT GGA AAA GGC AAT
hPtFP     61  AGC GTG GAG GGC ATC GTG AAC AAC CAC GTG TTC AGC ATG GAG GGC TTC GGC AAG GGC AAC
                  *   *   *                   *       *   * **       *   *   *   *   *       *

          +1 Val Leu Phe Gly Asn Gln Leu Met Gln Ile Arg Val Thr Lys Gly Gly Pro Leu Pro Phe
PtFP     121  GTA TTA TTT GGA AAC CAA TTG ATG CAA ATC CGG GTT ACA AAG GGA GGT CCG TTG CCA TTC
hPtFP    121  GTG CTG TTC GGC AAC CAG CTG ATG CAG ATC CGG GTG ACC AAG GGC GGC CCT CTG CCC TTC
               * * *   *   *       * *         *             *   *       *   *   * *     *

          +1 Ala Phe Asp Ile Val Ser Ile Ala Phe Gln Tyr Gly Asn Arg Thr Phe Thr Lys Tyr Pro
PtFP     181  GCT TTC GAT ATT GTT TCC ATA GCT TTC CAA TAC GGG AAT CGC ACT TTC ACG AAA TAC CCA
hPtFP    181  GCC TTC GAC ATC GTG AGC ATC GCC TTC CAG TAC GGC AAC CGG ACC TTC ACC AAG TAT CCC
               *       *   *   * **    *   *       *       *   *   *   *       *   *   *   *

          +1 Asp Asp Ile Ala Asp Tyr Phe Val Gln Ser Phe Pro Ala Gly Phe Phe Tyr Glu Arg Asn
PtFP     241  GAC GAC ATT GCG GAC TAC TTT GTT CAA TCA TTC CCG GCT GGA TTT TTC TAC GAA AGA AAT
hPtFP    241  GAC GAC ATC GCC GAC TAC TTC GTG CAG AGC TTC CCT GCC GGC TTC TTC TAC GAG CGG AAC
                   *   *           *   *   * ***       *   *   *   *           * * *   *

          +1 Leu Arg Phe Glu Asp Gly Ala Ile Val Asp Ile Arg Ser Asp Ile Ser Leu Glu Asp Asp
PtFP     301  CTA CGC TTT GAA GAT GGC GCC ATT GTT GAC ATT CGT TCA GAT ATA AGT TTA GAA GAT GAT
hPtFP    301  CTG CGG TTC GAG GAC GGC GCC ATC GTG GAC ATC CGG AGC GAC ATC AGC CTG GAG GAC GAC
               * * *   *   *   *           *   *       *   * ***   *   *   * * *   *   *   *

          +1 Lys Phe His Tyr Lys Val Glu Tyr Arg Gly Asn Gly Phe Pro Ser Asn Gly Pro Val Met
PtFP     361  AAG TTC CAC TAC AAA GTG GAG TAT AGA GGC AAC GGT TTC CCT AGT AAC GGA CCC GTG ATG
hPtFP    361  AAG TTC CAC TAC AAG GTG GAG TAC CGC GGC AAC GGC TTC CCT AGC AAC GGC CCT GTG ATG
                           *           * * *           *           *       *   *

          +1 Gln Lys Ala Ile Leu Gly Met Glu Pro Ser Phe Glu Val Val Tyr Met Asn Ser Gly Val
PtFP     421  CAA AAA GCC ATC CTC GGC ATG GAG CCA TCG TTT GAG GTG GTC TAC ATG AAC AGC GGC GTT
hPtFP    421  CAG AAG GCC ATC CTG GGC ATG GAG CCC AGC TTC GAG GTG GTG TAC ATG AAC AGC GGC GTG
               *   *           *               * ***   *                                   *

          +1 Leu Val Gly Glu Val Asp Leu Val Tyr Lys Leu Glu Ser Gly Asn Tyr Tyr Ser Cys His
PtFP     481  CTG GTG GGC GAA GTA GAT CTC GTT TAC AAA CTC GAG TCA GGG AAC TAT TAC TCG TGC CAC
hPtFP    481  CTG GTG GGC GAG GTG GAC CTG GTG TAC AAG CTG GAG AGC GGC AAC TAC TAC AGC TGC CAC
                       *   *   *   *   *       *   *       ***           *     ***

          +1 Met Lys Thr Phe Tyr Arg Ser Lys Gly Gly Val Lys Glu Phe Pro Glu Tyr His Phe Ile
PtFP     541  ATG AAA ACG TTT TAC AGA TCC AAA GGT GGA GTG AAA GAA TTC CCG GAA TAT CAC TTT ATC
hPtFP    541  ATG AAG ACC TTC TAC CGG AGC AAG GGC GGC GTG AAG GAG TTC CCT GAG TAC CAC TTC ATC
                   *   *   *       * * **   *   *   *       *   *       *   *   *       *

          +1 His His Arg Leu Glu Lys Thr Tyr Val Glu Glu Gly Ser Phe Val Glu Gln His Glu Thr
PtFP     601  CAT CAT CGT CTG GAG AAA ACC TAC GTG GAA GAA GGA AGC TTC GTG GAA CAA CAC GAG ACG
hPtFP    601  CAC CAC CGG CTG GAG AAG ACC TAC GTG GAG GAG GGC AGC TTC GTG GAG CAG CAC GAG ACC
               *   *   *           *               *   *   *               *   *           *

          +1 Ala Ile Ala Gln Leu Thr Thr Ile Gly Lys Pro Leu Gly Ser Leu His Glu Trp Val ***
PtFP     661  GCC ATT GCA CAA CTG ACC ACA ATT GGA AAA CCT CTG GGC TCC CTT CAT GAA TGG GTG TAG
hPtFP    661  GCC ATC GCC CAG CTG ACC ACC ATC GGC AAG CCT CTG GGC AGC CTG CAC GAG TGG GTG TAA
               *   *   *           *   *   *   *               **    *   *   *           *
```

Figure 10

```
    HindIII
    ~~~~~~~
+1                      M   V   N   R   N   V   L   K   N   T   G
1   AAG CTT GCC ACC ATG GTG AAC CGG AAC GTG CTG AAG AAC ACC GGC
    TTC GAA CGG TGG TAC CAC TTG GCC TTG CAC GAC TTC TTG TGG CCG

+1   L   K   E   I   M   S   A   K   A   S   V   E   G   I   V
46  CTG AAG GAG ATC ATG AGC GCC AAG GCC AGC GTG GAG GGC ATC GTG
    GAC TTC CTC TAG TAC TCG CGG TTC CGG TCG CAC CTC CCG TAG CAC

+1   N   N   H   V   F   S   M   E   G   F   G   K   G   N   V
91  AAC AAC CAC GTG TTC AGC ATG GAG GGC TTC GGC AAG GGC AAC GTG
    TTG TTG GTG CAC AAG TCG TAC CTC CCG AAG CCG TTC CCG TTG CAC

+1   L   F   G   N   Q   L   M   Q   I   R   V   T   K   G   G
136 CTG TTC GGC AAC CAG CTG ATG CAG ATC CGG GTG ACC AAG GGC GGC
    GAC AAG CCG TTG GTC GAC TAC GTC TAG GCC CAC TGG TTC CCG CCG

+1   P   L   P   F   A   F   D   I   V   S   I   A   F   Q   Y
181 CCT CTG CCC TTC GCC TTC GAC ATC GTG AGC ATC GCC TTC CAG TAC
    GGA GAC GGG AAG CGG AAG CTG TAG CAC TCG TAG CGG AAG GTC ATG

+1   G   N   R   T   F   T   K   Y   P   D   D   I   A   D   Y
226 GGC AAC CGG ACC TTC ACC AAG TAT CCC GAC GAC ATC GCC GAC TAC
    CCG TTG GCC TGG AAG TGG TTC ATA GGG CTG CTG TAG CGG CTG ATG

+1   F   V   Q   S   F   P   A   G   F   F   Y   E   R   N   L
271 TTC GTG CAG AGC TTC CCT GCC GGC TTC TTC TAC GAG CGG AAC CTG
    AAG CAC GTC TCG AAG GGA CGG CCG AAG AAG ATG CTC GCC TTG GAC

+1   R   F   E   D   G   A   I   V   D   I   R   S   D   I   S
316 CGG TTC GAG GAC GGC GCC ATC GTG GAC ATC CGG AGC GAC ATC AGC
    GCC AAG CTC CTG CCG CGG TAG CAC CTG TAG GCC TCG CTG TAG TCG

+1   L   E   D   D   K   F   H   Y   K   V   E   Y   R   G   N
361 CTG GAG GAC GAC AAG TTC CAC TAC AAG GTG GAG TAC CGC GGC AAC
    GAC CTC CTG CTG TTC AAG GTG ATG TTC CAC CTC ATG GCG CCG TTG

+1   G   F   P   S   N   G   P   V   M   Q   K   A   I   L   G
406 GGC TTC CCT AGC AAC GGC CCT GTG ATG CAG AAG GCC ATC CTG GGC
    CCG AAG GGA TCG TTG CCG GGA CAC TAC GTC TTC CGG TAG GAC CCG

+1   M   E   P   S   F   E   V   V   Y   M   N   S   G   V   L
451 ATG GAG CCC AGC TTC GAG GTG GTG TAC ATG AAC AGC GGC GTG CTG
    TAC CTC GGG TCG AAG CTC CAC CAC ATG TAC TTG TCG CCG CAC GAC

+1   V   G   E   V   D   L   V   Y   K   L   E   S   G   N   Y
496 GTG GGC GAG GTG GAC CTG GTG TAC AAG CTG GAG AGC GGC AAC TAC
    CAC CCG CTC CAC CTG GAC CAC ATG TTC GAC CTC TCG CCG TTG ATG

+1   Y   S   C   H   M   K   T   F   Y   R   S   K   G   G   V
```

Figure 10 (continued)

```
541   TAC AGC TGC CAC ATG AAG ACC TTC TAC CGG AGC AAG GGC GGC GTG
      ATG TCG ACG GTG TAC TTC TGG AAG ATG GCC TCG TTC CCG CCG CAC

 +1    K   E   F   P   E   Y   H   F   I   H   H   R   L   E   K
586   AAG GAG TTC CCT GAG TAC CAC TTC ATC CAC CAC CGG CTG GAG AAG
      TTC CTC AAG GGA CTC ATG GTG AAG TAG GTG GTG GCC GAC CTC TTC

 +1    T   Y   V   E   E   G   S   F   V   E   Q   H   E   T   A
631   ACC TAC GTG GAG GAG GGC AGC TTC GTG GAG CAG CAC GAG ACC GCC
      TGG ATG CAC CTC CTC CCG TCG AAG CAC CTC GTC GTG CTC TGG CGG

 +1    I   A   Q   L   T   T   I   G   K   P   L   G   S   L   H
676   ATC GCC CAG CTG ACC ACC ATC GGC AAG CCT CTG GGC AGC CTG CAC
      TAG CGG GTC GAC TGG TGG TAG CCG TTC GGA GAC CCG TCG GAC GTG

                          NotI
                       ~~~~~~~~~~
 +1    E   W   V   *
721   GAG TGG GTG TAA AGC GGC CGC
      CTC ACC CAC ATT TCG CCG GCG
```

The coding sequence (from start codon to stop codon):

atggtgaaccggaacgtgctgaagaacaccggcctgaaggagatcatgagcgccaag
gccagcgtggagggcatcgtgaacaaccacgtgttcagcatggagggcttcggcaag
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Figure 11

aagcttgccaccatggtgaaccggaacgtgctgaagaacaccggcctgaaggagatc
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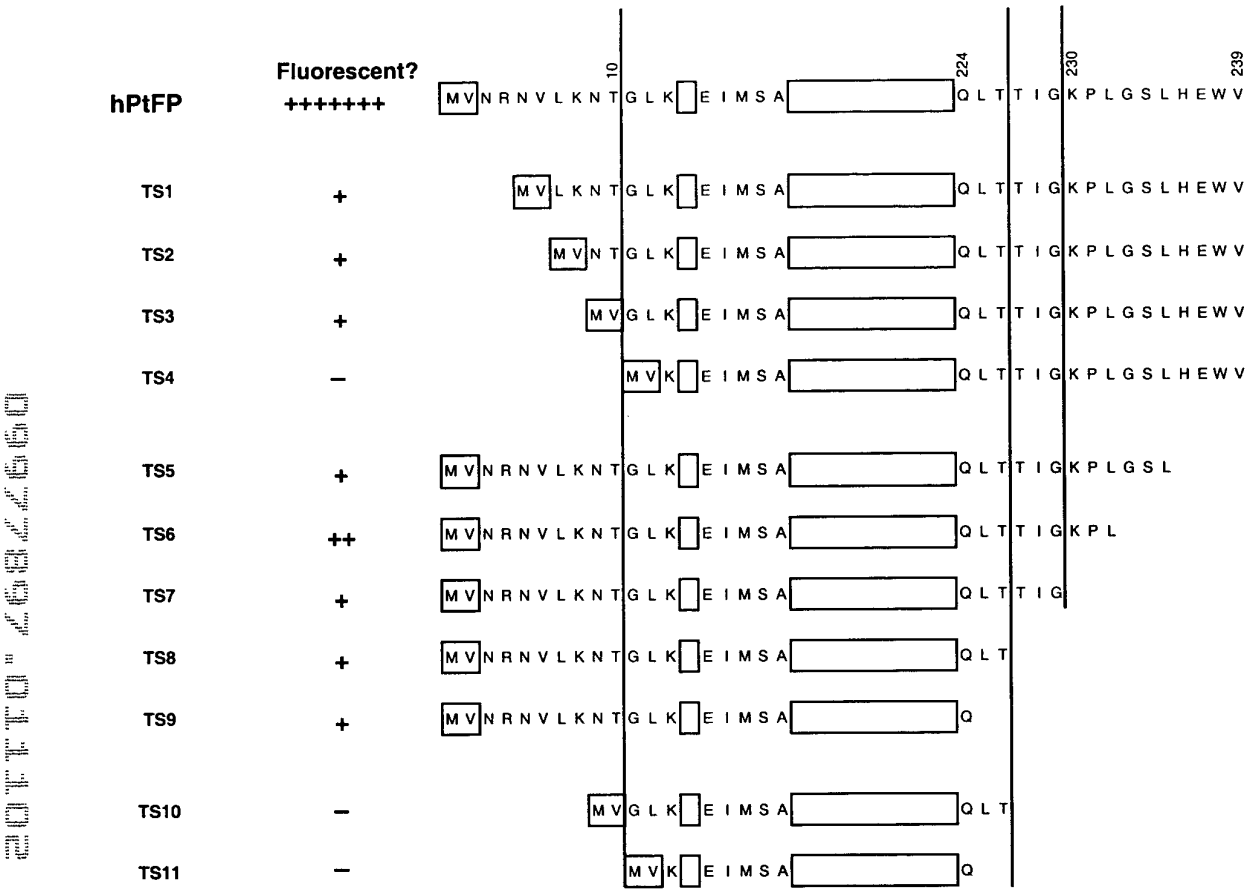
Figure 12

Figure 13



SUBSTITUTE SHEET (RULE 26)

Figure 14

no treatment

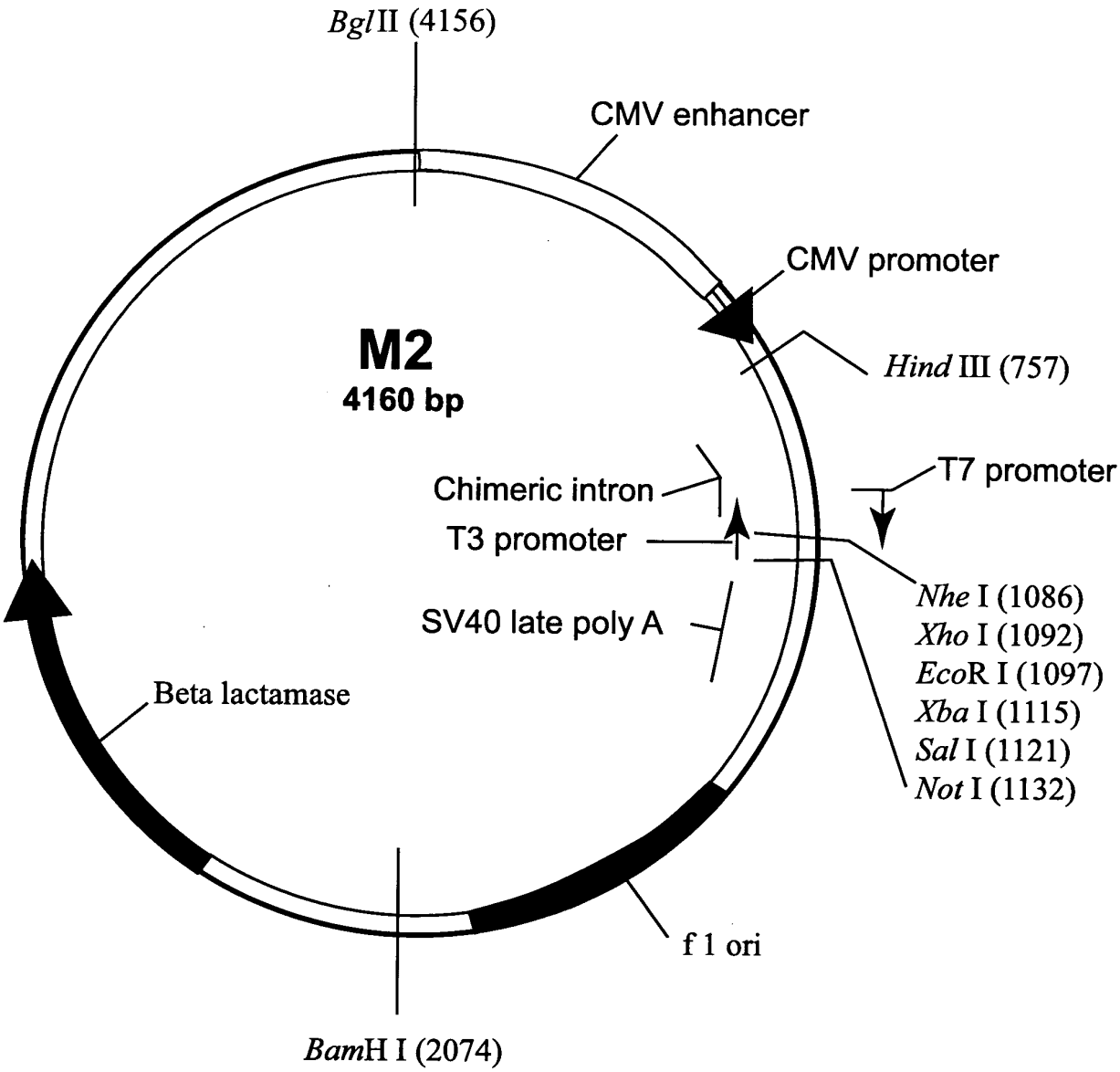
Staurosporine
10 nM 6 hours

Staurosporine
1 nM 24 hours

UUU F 0.45 (185619)	UCU S 0.18 (161556)	UAU Y 0.43 (133427)	UGU C 0.45 (108740)
UUC F 0.55 (225633)	UCC S 0.22 (192616)	UAC Y 0.57 (174805)	UGC C 0.55 (134523)
UUA L 0.07 (79303)	UCA S 0.15 (128429)	UAA * 0.29 (8187)	UGA * 0.50 (14381)
UUG L 0.13 (135218)	UCG S 0.06 (49456)	UAG * 0.21 (5913)	UGG W 1.00 (142435)
CUU L 0.13 (139009)	CCU P 0.28 (189374)	CAU H 0.41 (113684)	CGU R 0.08 (51100)
CUC L 0.20 (210903)	CCC P 0.33 (219428)	CAC H 0.59 (162826)	CGC R 0.19 (118404)
CUA L 0.07 (75667)	CCA P 0.27 (182506)	CAA Q 0.26 (130857)	CGA R 0.11 (68664)
CUG L 0.40 (435317)	CCG P 0.11 (76684)	CAG Q 0.74 (377006)	CGG R 0.21 (126679)
AUU I 0.35 (174021)	ACU T 0.24 (140780)	AAU N 0.46 (186915)	AGU S 0.15 (131222)
AUC I 0.49 (240138)	ACC T 0.36 (213626)	AAC N 0.54 (218376)	AGC S 0.24 (211962)
AUA I 0.16 (78463)	ACA T 0.28 (162837)	AAA K 0.42 (262630)	AGA R 0.20 (125600)
AUG M 1.00 (244236)	ACG T 0.12 (69346)	AAG K 0.58 (359627)	AGG R 0.20 (123646)
GUU V 0.18 (119013)	GCU A 0.26 (202329)	GAU D 0.46 (245435)	GGU G 0.16 (118798)
GUC V 0.24 (160764)	GCC A 0.40 (310626)	GAC D 0.54 (287040)	GGC G 0.34 (250410)
GUA V 0.11 (76398)	GCA A 0.23 (173010)	GAA E 0.42 (317703)	GGA G 0.25 (180955)
GUG V 0.47 (317359)	GCG A 0.11 (82647)	GAG E 0.58 (441298)	GGG G 0.25 (180001)

Figure 15

Figure 16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CMV enhancer
CMV promoter
M2
4160 bp
Hind III (757)
T7 promoter
Chimeric intron
T3 promoter
Nhe I (1086)
Xho I (1092)
EcoR I (1097)
Xba I (1115)
Sal I (1121)
Not I (1132)
SV40 late poly A
Beta lactamase
f 1 ori
BamH I (2074)

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Figure 17

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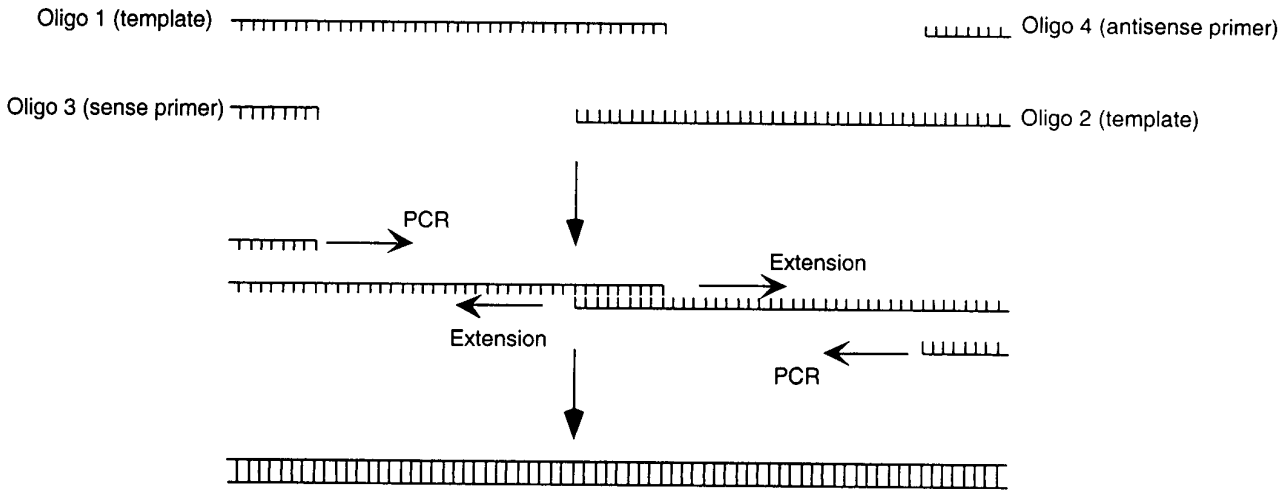
Figure 17 (continued)

Figure 18


Oligo 1 (template)
Oligo 4 (antisense primer)
Oligo 3 (sense primer)
Oligo 2 (template)
PCR
Extension
Extension
PCR